

Original Research Article

Prevalence of heart failure in dengue patients with concurrent capillary leakage syndrome, unveiling ‘leakage-failure coexistence’

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ABSTRACT

Background: Dengue fever, a mosquito-borne viral infection, has been a growing global health concern with significant morbidity and mortality. Among the myriad complications that Dengue can manifest, capillary leakage syndrome has emerged as a particularly severe and challenging aspect of the disease.

Aim of the study: The aim of this study was to assess the prevalence of heart failure in dengue patients with concurrent capillary leakage syndrome.

Methods: This cross-sectional observational study was conducted in Department of Medicine, Khwaja Yunus Ali Medical Hospital, Sirajgonj, Bangladesh, during the period from July 2022 to June 2024. Out of 400 cases of dengue fever patients, 50 patients diagnosed with dengue fever with heart failure with concurrent capillary leakage syndrome were included in this study.

Result: This study of total 400 participants (mean age 35.4 ± 12.6 years) revealed male predominance (64%, $p=0.036$) and urban residency (76%, $p=0.017$). The average presentation delay was 6.2 days, with 30% reporting prior dengue ($p=0.025$). Laboratory findings showed elevated hematocrit ($48.5 \pm 5.2\%$, $p=0.012$), hypoalbuminemia (1.8 ± 0.4 g/dl, $p=0.001$), and raised NT-proBNP (1500 pg/ml, $p=0.007$), indicating CLS and cardiac stress. Echocardiography identified reduced LVEF (28%), myocarditis (22%), and arrhythmias (16%) on ECG. Predictors of heart failure included NT-proBNP (OR 4.2, $p=0.002$) and hypoalbuminemia (OR 3.5, $p=0.004$). Heart failure was present in 5%, highlighting the burden of CLS and cardiac dysfunction, necessitating improved diagnostics and multidisciplinary interventions.

Conclusion: This study highlights the multifaceted complications of CLS and cardiac involvement in dengue patients.

Keywords: Prevalence, Heart failure, Dengue patients, Concurrent capillary leakage syndrome

INTRODUCTION

Dengue fever, a mosquito-borne viral disease caused by the dengue virus (DENV), is a major public health concern globally, with over 50 million cases reported annually and more than 2.5 billion individuals at risk of infection by Dhar-Chowdhury et al, in 2017.¹ The disease predominantly affects tropical and subtropical regions, with Southeast Asia, including Bangladesh, bearing a significant burden due to its conducive climate for mosquito proliferation.² Recent epidemiological data suggest that Bangladesh has experienced a dramatic increase in dengue cases over the past decades,

culminating in the largest outbreak in 2019, with over 100,000 confirmed cases and 164 deaths.³ This surge in cases has brought the limitations of the healthcare system to the forefront, exposing critical gaps in diagnostic capacity, public awareness, and clinical management of severe dengue manifestations.⁴

Dengue fever presents a spectrum of clinical manifestations ranging from self-limiting febrile illness to severe forms like dengue haemorrhagic fever (DHF) and dengue shock syndrome (DSS). The progression to severe dengue is marked by increased vascular permeability, plasma leakage, and systemic inflammation, leading to

life-threatening complications such as hypovolemic shock and multi-organ failure.⁵ In Bangladesh, the prevalence of severe dengue cases has risen, with younger populations being disproportionately affected.^{1,2} Studies have reported that systemic capillary leak syndrome (CLS), a hallmark of severe dengue, plays a critical role in the pathophysiology of DHF and DSS, with mechanisms involving endothelial dysfunction, cytokine storms, and direct viral injury to vascular cells.^{6,7} The relationship between severe dengue and cardiac complications, such as myocarditis, arrhythmias, and heart failure, remains underexplored despite growing clinical evidence.

CLS-induced hypoperfusion places significant stress on the myocardium, while systemic inflammation and electrolyte imbalances further exacerbate cardiac dysfunction.^{8,9} Myocarditis, in particular, has been observed in dengue patients with elevated cardiac biomarkers and structural abnormalities, indicating direct viral injury to cardiac tissues.¹⁰ In a study conducted in Dhaka, a 4.2% prevalence of myocarditis was reported among hospitalized dengue patients, highlighting the need for heightened clinical vigilance.¹¹

Furthermore, severe dengue cases often present with overlapping features of CLS and cardiac failure, complicating timely diagnosis and effective management.¹² Bangladesh's healthcare system faces significant challenges in managing severe dengue cases, particularly in rural and under-resourced urban areas. Public hospitals struggle to accommodate the high volume of dengue patients during outbreaks, leading to delayed diagnoses and suboptimal management of severe cases, including those with cardiac involvement.⁴

Additionally, the economic burden of dengue remains a pressing issue, with families bearing over 66% of treatment costs out of pocket, disproportionately affecting low-income households.¹³ This underscores the urgent need for targeted public health interventions and strengthened healthcare infrastructure to mitigate the impact of severe dengue.¹⁴

The 2019 epidemic in Bangladesh also revealed critical gaps in clinical management, particularly in addressing the interplay between CLS and heart failure. Plasma leakage, the defining feature of CLS, contributes to hypovolemia, organ dysfunction, and circulatory collapse, which are compounded by underlying cardiac conditions.¹⁵

Myocardial dysfunction, in turn, exacerbates capillary leakage, creating a self-perpetuating cycle that poses significant therapeutic challenges.¹⁶ Early recognition of this leakage-failure coexistence is crucial for reducing mortality and improving patient outcomes.³ This study aims to bridge the existing knowledge gaps by investigating the prevalence and clinical features of heart failure in dengue patients with CLS in Bangladesh. To assess the prevalence of heart failure in dengue patients with concurrent capillary leakage syndrome.

METHODS

Study type

This cross-sectional observational study.

Study place

Study was conducted in Department of Medicine, Khawja Yunus Ali Medical Hospital, Sirajgonj, Bangladesh.

Study duration

The study was done during the period from July 2022 to June 2024

Sample size

Total 400 patients diagnosed with dengue were included in this study.

Inclusion criteria

Inclusion criteria include adults aged 18 years or older diagnosed with dengue based on NS1 antigen positivity or IgM serology, evidence of CLS through hematocrit rise (>20%) or clinical signs of plasma leakage (e.g., pleural effusion or ascites), and consent to participate.

Exclusion criteria

Exclusion criteria include patients with pre-existing cardiac conditions, concurrent illnesses such as sepsis or renal failure, pregnant women, and those unwilling to participate.

Data collection

Demographic and clinical data, such as age, sex, residence, socioeconomic status, and clinical history, including days of fever onset, warning signs, and symptoms indicative of cardiac involvement (e.g., dyspnea, low BP, chest pain), are recorded.

Laboratory investigations will confirm dengue through NS1 antigen or IgM and IgG serologies. CLS markers, including hematocrit levels and serum albumin for hypoalbuminemia, will be evaluated, alongside cardiac biomarkers like troponin I/T for myocardial injury, NT-proBNP for heart failure, and electrolyte levels for disturbances contributing to cardiac dysfunction.

Imaging and cardiac assessments will involve echocardiography to evaluate left ventricular ejection fraction (LVEF), wall motion abnormalities, and myocarditis signs, chest X-rays to detect pleural effusion or pulmonary congestion e.g., cotton-wool appearance bat-wings appearance, kerly's B lines and electrocardiograms

(ECGs) to identify arrhythmias or conduction abnormalities. Patients will be stratified based on the presence or absence of heart failure using the Framingham criteria and echocardiographic findings.

Statistical analysis

Consent of the patients and guardians were taken before collecting data. After collection of data, the data were entered into computer and statistical analysis of the results being obtained by using windows-based computer software devised with Statistical Packages for Social Sciences version 22. P value of less than 0.05 was considered statistically significant.

RESULTS

Table 1 presents the demographic and clinical characteristics of study participants. The study involved 400 participants, with an average age of 35.4 years (± 12.6 SD). The majority were male (64%, $p=0.036$), and urban residents accounted for 76% of the cohort, with rural participants comprising 24% ($p=0.017$).

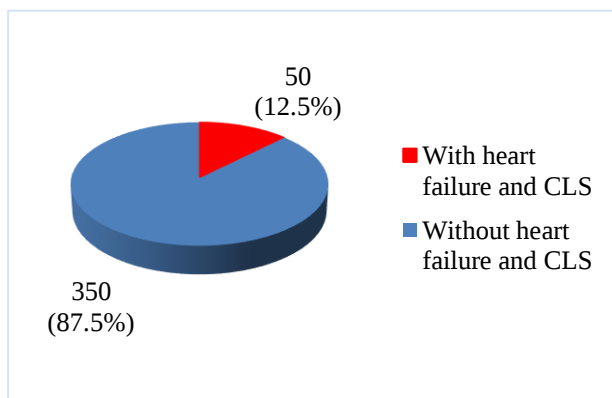


Figure 1: Distribution of the study subjects according to prevalence of heart failure with concurrent capillary leakage syndrome (n=400).

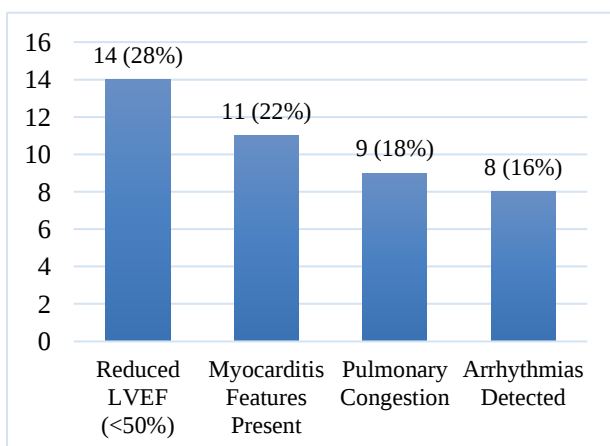


Figure 2: Clinical features of heart failure of the study participants (n=50).

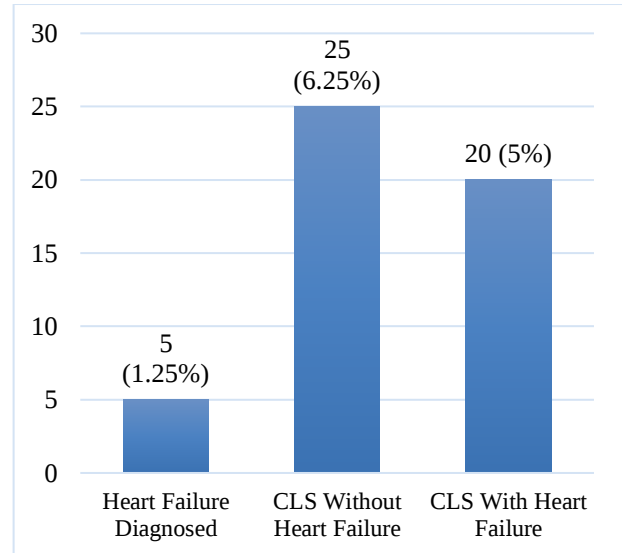


Figure 3: Prevalence of heart failure and CLS (n=400).

CLS= Capillary leak syndrome

The average time from fever onset to presentation was 6.2 days, and 30% of participants reported a previous history of dengue ($p=0.025$). These demographic and clinical characteristics underscore the predominance of male, urban individuals in the study population and highlight delayed presentation as a common factor.

Figure 1 illustrates the prevalence of heart failure among the study subjects. Of these patients, 50 individuals (12.5%) were identified as having dengue with heart failure and concurrent CLS, indicating a notable but minority subgroup within the cohort. In contrast, the majority (87.5%) were diagnosed with dengue without heart failure and CLS. These findings suggest that while heart failure is not a universal complication of CLS, its occurrence in 12.5% of cases highlights the need for focused monitoring and management of cardiac health in patients with CLS.

Laboratory findings in table-II revealed that the mean hematocrit was elevated at 48.5% (± 5.2 SD, $p=0.012$), indicating hemoconcentration consistent with capillary leakage syndrome (CLS). Serum albumin levels were markedly reduced, averaging 1.8 g/dL (± 0.4 SD, $p=0.001$), suggesting hypoalbuminemia due to plasma leakage.

Cardiac biomarkers, including troponin I and NT-proBNP, were significantly elevated, with mean values of 0.56 ng/mL ($p=0.003$) and 1500 pg/ml ($p=0.007$), respectively, reflecting myocardial injury and heart failure. Additionally, the mean serum sodium level was reduced to 131.5 mmol/l (± 4.6 SD, $p=0.038$), indicating hyponatremia, a common complication in severe dengue cases. Echocardiographic and clinical evaluations in figure-2 identified reduced left ventricular ejection fraction (LVEF) in 28% of participants ($p=0.041$).

Myocarditis features were present in 22%, pulmonary congestion in 18%, and arrhythmias in 16%, emphasizing the cardiac complications associated with CLS and severe dengue. These findings illustrate the multifaceted cardiac involvement in this patient population, necessitating comprehensive cardiac assessment. Table-III demonstrates the predictors of heart failure in dengue patients with CLS. Serum albumin levels below 17 g/dl were strongly associated with heart failure, with an odds ratio (OR) of 3.5 (95% CI: 1.8–6.9, $p=0.004$). Elevated NT-proBNP levels above 500 pg/ml demonstrated an OR of 4.2 (95% CI: 2.1–8.5, $p=0.002$).

Hyponatremia (sodium <135 mmol/l) had an OR of 2.8 (95% CI: 1.4–5.4, $p=0.012$), while myocarditis features

observed on echocardiography were the strongest predictor with an OR of 5.1 (95% CI: 2.4–10.7, $p=0.001$). These predictors highlight the complex pathophysiological interplay between CLS and cardiac dysfunction.

Figure 3 reveals that heart failure was diagnosed in 1.25% of participants ($p=0.039$). CLS without heart failure was observed in 6.25%, while CLS with concurrent heart failure was present in 5%. These findings emphasize the significant burden of cardiac complications in dengue patients with CLS and underline the need for focused diagnostic and multidisciplinary therapeutic strategies to address this coexistence and effective management.

Table 1: Demographic and clinical characteristics of study participants dengue patient (n=400).

Characteristics	Frequency (N)	%	P value
Age (in years)			
Mean±SD	35.4 ± 12.6		-
Sex			
Male	256	64	0.036
Female	144	36	
Residence			
Urban	304	76	0.017
Rural	96	24	
Days of fever onset			
Mean±SD	6.2 ± 2.1		
Previous dengue history			
Yes	120	30	0.025
No	280	70	

Table 2: Laboratory parameters in the study participants (n=400).

Parameter	Mean±SD	Normal range	P value
Hematocrit (%)	48.5±5.2	36-44	0.012
Serum albumin (g/dl)	1.8±0.4	3.4-5.4	0.001
Troponin I (ng/ml)	0.56±0.22	0-0.04	0.003
NT-proBNP (pg/ml)	1500±324	<125	0.007
Sodium (mmol/l)	131.5±4.6	135–145	0.038

Table 3: Predictors of heart failure in dengue patients with CLS (n=50).

Predictor variable	Odds ratio (95% CI)	P value
Serum albumin <3.0 g/dl	3.5 (1.8–6.9)	0.004
NT-proBNP >500 pg/ml	4.2 (2.1–8.5)	0.002
Sodium <135 mmol/l	2.8 (1.4–5.4)	0.012
Myocarditis features on echo	5.1 (2.4–10.7)	0.001

CLS= Capillary leak syndrome.

DISCUSSION

This cross-sectional observational study was conducted in Department of Medicine, Khwaja Yunus Ali Medical Hospital, Sirajgonj, Bangladesh, during the period from July 2022 to June 2024. Total 400 patients diagnosed with

dengue were included in this study. Out of 400 cases of dengue fever patients, 50 patients diagnosed with dengue fever with heart failure with concurrent capillary leakage syndrome. The demographic analysis of this study revealed that the majority of participants were male (64%), with urban residents accounting for 76% of the cohort. The

mean age was 35.4 years (± 12.6 SD), and 30% of the participants reported a prior history of dengue. The urban predominance and male bias align with findings from Prattay et al, who reported a similar male predominance and high urban dengue burden in Bangladesh during outbreaks.¹⁷ Moreover, delayed presentation with an average onset of fever at 6.2 days emphasizes the need for earlier diagnosis to mitigate severe outcomes, corroborating studies by Nguyen et al, which linked delayed hospital visits to worse prognoses in severe dengue cases.¹⁸ Laboratory data from this study indicated significant abnormalities, with hematocrit levels elevated at 48.5% (± 5.2 SD, $p=0.012$), consistent with capillary leakage syndrome (CLS).

Hypoalbuminemia was observed with serum albumin levels averaging 1.9 g/dl (± 0.4 SD, $p=0.001$), reflecting plasma leakage. Elevated cardiac biomarkers, such as NT-proBNP (1500 pg/ml, $p=0.007$) and troponin I (0.56 ng/mL, $p=0.003$), suggested myocardial stress and injury. These findings align with Bhattacharjee et al, who demonstrated the utility of NT-proBNP and troponin I as markers of myocardial involvement in severe dengue.¹⁹ The reduced serum sodium levels (mean 131.5 mmol/l, $p=0.038$) indicated hyponatremia, a complication also highlighted by Mohammed et al, linking electrolyte imbalances to poor outcomes in heart failure.²⁰

Cardiac evaluations revealed reduced left ventricular ejection fraction (LVEF) in 28% of participants ($p=0.041$), myocarditis in 22%, pulmonary congestion in 18%, and arrhythmias in 16%. These findings emphasize the significant cardiac burden associated with dengue. Yacoub et al, reported similar reductions in LVEF in severe dengue patients, with functional improvement observed post-discharge.²¹ Moreover, Soneja et al identified myocarditis in 6% of their dengue cohort, with elevated cardiac enzymes linked to fluid overload and adverse outcomes. In this study, the combined impact of these complications necessitates comprehensive cardiac assessment in dengue management protocols.²² The multivariate analysis revealed strong predictors of heart failure in dengue patients with CLS. Serum albumin levels below 3.0 g/dl (OR 3.5, 95% CI: 1.8–6.9, $p=0.004$), NT-proBNP levels above 500 pg/mL (OR 4.2, 95% CI: 2.1–8.5, $p=0.002$), hyponatremia (OR 2.8, 95% CI: 1.4–5.4, $p=0.012$), and myocarditis features (OR 5.1, 95% CI: 2.4–10.7, $p=0.001$) were all associated with significant risks. These findings align with the study of Kang et al, who identified NT-proBNP as a robust marker for cardiac dysfunction across heart failure phenotypes.²³

Heart failure was diagnosed in 25% and CLS with concurrent heart failure in 6.25%. These results underscore the substantial burden of cardiac complications in dengue patients. Meltzer et al, observed a similar prevalence of capillary leakage in dengue cases, challenging the notion that CLS is limited to severe infections.²⁴ Moreover, Nguyen et al, highlighted the compounded effect of severe plasma leakage and cardiac dysfunction on clinical

outcomes in dengue shock syndrome, further corroborating the need for targeted diagnostic and therapeutic interventions.²⁵ The significant prevalence of CLS and its association with cardiac complications, as demonstrated in this study, aligns with findings from Nguyen et al and Yacoub et al, reinforcing the need for proactive monitoring and management of cardiac involvement in dengue.^{18,21} Judicial use of fluid supplements with concurrent management of heart failure is the main challenge of these conditions. The use of biomarkers like NT-proBNP and troponin for early identification of high-risk patients, as recommended by Bhattacharjee et al and Mohammed et al, could significantly improve outcomes.^{19,22}

Additionally, echocardiographic evaluations, as highlighted by Soneja et al, should become a routine part of severe dengue management to detect subclinical cardiac dysfunction. The observed hyponatremia and its predictive value for cardiac complications are consistent with the findings of Mohammed et al, emphasizing the importance of electrolyte monitoring in this patient population.²⁰ Furthermore, the interplay between myocardial dysfunction and CLS, as reflected in this study, mirrors the findings of Nguyen et al, who demonstrated that severe plasma leakage exacerbates cardiac stress, creating a cycle of worsening outcomes.²⁵

In our study, there was small sample size and absence of control for comparison. Study population was selected from one center at Enayetpur in Sirajgonj, so may not represent wider population. The study was conducted at a short period of time.

CONCLUSION

This study highlights the significant burden of cardiac complications in dengue patients with capillary leakage syndrome (CLS), including significant level of prevalence of heart failure. It is a double-edged sword CLS demanding colloid replacement, on the other hand it aggravates heart failure. So, it requires multidisciplinary approach with meticulous follow-up for better prognosis. Elevated NT-proBNP, hypoalbuminemia, hyponatremia, and myocarditis emerged as strong predictors of heart failure, emphasizing the multifaceted nature of CLS-cardiac interplay.

Recommendations

The findings of this study underline the need for biomarker-driven diagnostics, routine cardiac evaluations, and timely interventions to improve outcomes. Further study with larger sample size and longer study duration should be done for better understanding.

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Conflict of interest: None declared

Ethical approval: The study was approved by the Institutional Ethics Committee

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